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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/202,969      | 11/03/2003  | Jan Weiler           | SCHU 202 US-        | 3605             |

7590

07/31/2006

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| EXAMINER |
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LIU, SUE XU

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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1639

DATE MAILED: 07/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>09/202,969 | <b>Applicant(s)</b><br>WEILER ET AL. |  |
|                              | <b>Examiner</b><br>Sue Liu           | <b>Art Unit</b><br>1639              |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 July 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5 and 7-9 is/are pending in the application.
- 4a) Of the above claim(s) 8 and 9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 7 is/are rejected.
- 7) ☒ Claim(s) 1 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### Claim Status

Claim 6 has been canceled as filed on 12/23/1998;

Claims 1, and 3-5 have been amended as filed on 12/23/1998;

Claims 7-9 have been added;

Claims 1-5, and 7-9 are currently pending;

Claims 8 and 9 have been withdrawn;

Claims 1-5 and 7 are being examined in this application.

### *Election/Restrictions*

1. Applicant's election of Group I (claims 1-5 and 7) in the reply filed on 7/6/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 8 and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/6/06.

3. Applicant's election without traverse of the following species:

A.) NPEOC as the 3'succinate (Applicants elected the species in a supplemental response filed on 7/12/06);

B.) propylene as the matrix;

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C.) methylamino as the alkylamino group (Applicants elected the species in a supplemental response filed on 7/12/06)

in the replies filed on 7/6/06 and 7/12/06 are acknowledged.

***Priority***

4. This application is filed under 35 U.S.C 371 of PCT/DE97/01332 (filed on 06/24/1997).

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

However, it is noted that a certified translation of the foreign priority paper has not been filed.

**Sequence Rule Compliance**

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) below:

The instant disclosure recites lists of sequences on Pages 10 and 11 in the instant specification, but the application has failed to comply with the Sequence Rule (see the attached "Notice to Comply" for requirements on compliance).

***Specification***

7. The disclosure is objected to because of the following informalities:

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The instant specification contains pages (pages 10 and 11) not written in English, and appears to be a list of sequences. See above section regarding "Sequence Rule Compliance".

Appropriate correction is required.

### ***Claim Objections***

8. Claim 1 is objected to because of the following informalities: As pointed out in the previously sent Restriction Requirement, the said claim appears to contain a typo where the term "30'-succinate" should be "3'-succinate".

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-5 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the parallel synthesis" in line 1 of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 1 recites the phrase "attaching a 30'-succinate derivative of a protected nucleoside thereto" (emphasis added), which is in conflict with the preamble and the last step of the claim, where oligonucleotides (in plural) are recited to indicate parallel synthesis of multiple oligonucleotides.

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Claim 3 recites the limitation "the 3'-succinate derivative". There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

12. Claims 1, 3, 4, and 5 are rejected under 35 U.S.C. **102(b)** as being anticipated by Weiler et al (Nucleosides and Nucleotides. Vol. 14(3-5):917-920; 1995).

The instant claims recite a process for the parallel synthesis of oligonucleotides on an alkylamino modified matrix surface, comprising attaching a 3'-succinate derivative of a protected nucleoside thereto, and automatedly synthesizing oligonucleotide thereafter.

Weiler et al, throughout the publication, teach an improved method for large scale synthesis of oligonucleotides applying the NPE/NPEOC-strategy (see Title and Abstract of the reference). The reference teaches synthesizing oligonucleotides on proylamino derivatized polystyrene (see Figure 1 and pg 918, 2<sup>nd</sup> para.), which reads on synthesizing oligonucleotides on a alkylamino modified matrix surface of **clm 1**.

The reference also teaches loading appropriately protected 3'-succinyl nucleosides to derivatize the support (pg 918, 2<sup>nd</sup> para), which reads on attaching a 3'-succinate derivative of a protected nucleoside of **clm 1**.

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The reference also teaches using a standard DNA-synthesizer (ABI Model 392) to synthesize several desired oligonucleotides (pg 918, 3<sup>rd</sup> para), which is an automated DNA synthesizer with multiple columns (see pg 5-4 of the manual) as evidenced by the manufacturer's manual to the instrument (Quick Reference Guide 392/394 DNA/RNA Synthesizers. Revision B; 10/1996. ABI). This reads on automated synthesis of oligonucleotides as recited in **clm 1** and multichannel synthesis chamber of **clm 4**.

The reference also teaches using NPE/NPEOC protected nucleosides to synthesize oligomers such as a tetramer, d(GTAC), (see pg 918), which reads on the nucleotides listed in **clm 3**.

The reference also teaches using polystyrene as the matrix for oligonucleotide synthesis (Figure 1 and pg 918, 2<sup>nd</sup> para.), which reads on the polymer matrix of **clm 5**.

13. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Weiler et al (Innovation Perspect. Solid Phase Synth. Collect. Pap., Int. Symp., 3rd (1994), Meeting Date 1993, pg 131-134. Editor(s): Epton, Roger. Mayflower Worldwide Ltd.: Birmingham, UK.).

Weiler et al, throughout the publication, teach an improved method for large scale synthesis of oligonucleotides applying the NPE/NPEOC-strategy (see 2<sup>nd</sup> para. on pg 131). The reference teaches synthesizing oligonucleotides on methylamino derivatized TetraGel (a polystyrene matrix) (see Figure 1 and 2 on pg 132), which reads on synthesizing oligonucleotides on a methylamino modified polymer matrix surface of **clms 1, 2, and 5**.

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The reference also teaches loading appropriately protected 3'-succinate nucleosides to the support (pg 132, Figure 1 and 2), which reads on attaching a 3'-succinate derivative of a protected nucleoside of **clm 1**.

The reference also teaches using a standard DNA-synthesizer (ABI Model 392) to synthesize several desired oligonucleotides (pg 918, 3<sup>rd</sup> para), which is an automated DNA synthesizer with multiple columns (see pg 5-4 of the manual) as evidenced by the manufacturer's manual to the instrument (Quick Reference Guide 392/394 DNA/RNA Synthesizers. Revision B; 10/1996). This reads on automated synthesis of oligonucleotides as recited in **clm 1** and multichannel synthesis chamber of **clm 4**.

The reference also teaches using NPE/NPEOC protected nucleosides to synthesize oligomers (see pg 132, Figure 1 and 2), which reads on the nucleotides listed in **clm 3**.

### *Claim Rejections - 35 USC § 103*

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).



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15. Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being obvious over Matson et al (US 5,429,807; 7/4/1995), Meldal et al (US Patent 5,352,756; 10/4/1994), and Pfeleiderer et al (US Patent 5,652,358; 1997; filed 11/3/1994).

**Matson et al**, throughout the patent, teaches an automated method and apparatus for performing biopolymers (oligonucleotide) synthesis (see Abstract of the reference), which reads on the automated synthesis of **clm 1**. The reference teaches that the solid support for attaching polynucleotides is polypropylene (see Claim 20 of the reference), which reads on the polypropylene polymer matrix of **clms 1, 5, and 7**. The reference also teaches parallel polynucleotide syntheses with a plurality of parallel channels (col. 3, lines 45+ and Claims 15 and 20 of the reference), which read on the multichannel synthesis chamber with fixed matrix, as recited in **clm 4**.

Matson et al do not specifically teach the polymer matrix is modified with methylamino groups as recited in **clm 2**. The reference also does not teach the nucleosides used for the synthesis are 3'-succinate derivatives of NPEOC protected nucleosides as recited in **clms 1 and 3**.

However, **Meldal**, throughout the patent, teaches polypropylene glycol-containing polymer designed for the application of a solid support for the oligonucleotide synthesis (see Abstract of the reference). The reference also teaches that the polymers are incorporated with a spacer comprising a functional group such as alkylamino for attaching the nucleotides to the polymer (see Abstract and Claims 1-3 of the reference), which reads on the polypropylene polymer and the alkylamino of **clms 1, 5 and 7**. The reference also teaches a spacer linked to the

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polymer comprises a methylamino group (see Figure 2 and Claim 4, formula II of the reference), which reads on the methylamino group modified matrix surface, as recited in **clm 2**.

**Pfleiderer et al**, throughout the patent, teach methods of preparing oligonucleotides and oligoribonucleotides using nucleosides with various protective groups by solid state synthesis (see Abstract and lines 39+). The reference teaches various 3'-succinate derivative of protected nucleosides (col. 10, lines 42+), where the protective group for the nucleoside can be para-nitrophenylethyloxycarbonyl group (col. 7, lines 32+). The reference also teaches that the succinic acidresidue in the 3' position acts as linker to the polymeric support used in synthesis of the oligoes (col. 10, lines 60+). These read on the synthesis of oligonucleotides on a matrix comprising attaching a 3'-succinate derivative of a protected nucleoside, as recited in **clm 1**.

The reference also teaches various 3'-succinate derivatives such as 2'-O-(1-benzyloxyethyl)-5'-DMTR-N<sup>4</sup>-NPEOC-3'-O-succinylcytidine (col. 24, lines 49+), which reads on dC<sup>NPEOC</sup> of **clm 3**. The reference also teaches other modified 3'-succinate derivatives of protected nucleosides including modified adenosine (col. 26, lines 50), modified guanosine (col. 28, lines 45), and modified thymidine (see Claims 1-5, for example), which read on the various modified nucleosides recited in **clm 3**. The reference also teaches various modified nucleosides such as the one with formula I (top of col 3) and which can have various nucleosides including a A, T, G, C (col. 3, lines 30+), and fluorescein label (col. 5, lines 42+, and col. 13). This reads on the fluorescein labeled dC of **clm 3**.

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use polypropylene matrix derivatized with methylamino

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groups and 3'-succinate derivative of protected nucleosides for automated polynucleotide or oligonucleotide synthesis.

A person of ordinary skill in the art would have been motivated at the time of the invention to use methylamino group modified polypropylene matrix to synthesize oligonucleotides, because solid state synthesis of oligonucleotides require modifying the solid support (matrix) to attach the synthesized oligonucleotides as taught by both Matson et al (who teach derivatizing the solid support for attaching polynucleotide in Column 5, lines 40+), and Meldal teaches using polypropylene polymer comprising methylamino group for attaching oligonucleotides thereon as discussed above.

A person of ordinary skill in the art would have been motivated at the time of the invention to use 3'-succinate derivative of protected nucleosides to synthesize oligonucleotides, because Pflieger et al teach a fundamental problem in the chemical synthesis of DNA is to find suitable protective group for the amino and hydroxyl groups in the nucleoside bases (col.1, lines 7+), and the para-nitrophenylethoxycarbonyl group is a suitable and known protective group for nucleoside bases (col. 7, lines 30+ and col. 24, lines 40+). Due to the fact that the using succinic acid as a linker between the nucleoside and the polymer matrix is known in the art as taught by Pflieger et al (col. 10, lines 44+), a person of ordinary skill in the art would have been motivated to use succinate derivatives of protected nucleosides for solid state polynucleotide synthesis. A person of ordinary skill in the art would have been motivated at the time of the invention to use 3'-succinate derivative of fluorescein labeled nucleosides to synthesize oligonucleotides, because attaching fluorescein as labels onto polynucleotides are

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known in the art and the labeled polynucleotides can be used for various applications such as hybridization assays (col. 5, lines 41+ and col. 12, lines 56+) as taught by Pfeiderer et al.

An ordinary skilled artisan would have reasonable expectation of success of achieving such modifications since Meldal has demonstrated the successfully modification of polypropylene matrix with methylamino group and Pfeiderer et al have demonstrated the successful utilization of 3'-succinate derivative of protected nucleosides for solid state synthesis of polynucleotides.

16. Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being obvious over Matson et al (US 5,429,807; 7/4/1995), Meldal et al (US Patent 5,352,756; 10/4/1994), Kierzek et al (Biochemistry. Vol. 25: 7840-7846; 1986; cited previously in R/E), and Fernandez-Fornier et al (Nucleic Acids Research. Vol. 18: 5729-5734; 1990).

**Matson et al**, throughout the patent, teaches an automated method and apparatus for performing biopolymers (oligonucleotide) synthesis (see Abstract of the reference) as discussed supra.

Matson et al do not specifically teach the polymer matrix is modified with methylamino groups as recited in **clm 2**. The reference also does not teach the nucleosides used for the synthesis are 3'-succinate derivatives of NPEOC protected nucleosides as recited in **clms 1 and 3**.

However, **Meldal**, throughout the patent, teaches polypropylene glycol-containing polymer designed for the application of a solid support for the oligonucleotide synthesis, as discussed above.

**Kierzek et al**, throughout the publication, teach solid-phase synthesis of oligonucleotides using succinate derivatives (See page 7840, 3<sup>rd</sup> paragraph of right column of the reference). The reference teaches synthesis of nucleosides covalently attached to silica support using succinic anhydride, and producing 3'-succinate derivative of a protected nucleoside as shown in Figure 1 of the reference (see top of pg 7841). The instant specification also states "the 3'-succinate derivatives of protected nucleosides...as described in Kierzek et al..." (top, pg 3 of the instant specification. These read on the synthesis of oligonucleotides on a matrix comprising attaching a 3'-succinate derivative of a protected nucleoside, as recited in **clm 1**.

**Fernandez-Forner et al**, throughout the publication, teach synthesis solid state synthesis of oligodeoxynucleotide (see Abstract to the reference). The reference teaches NPE/NPEOC protected nucleosides including  $dG^{NPE,NPEOC}$ ,  $dC^{NPEOC}$  and  $dA^{NPEOC}$  (Figure 2 and pg 5731, left col., 2<sup>nd</sup> para. of the reference). The reference also teaches inclusion of dT molecules for generating oligonucleotides with T residues (see Table 3, for example).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use polypropylene matrix derivatized with methylamino groups and 3'-succinate derivative of protected nucleosides for automated polynucleotide or oligonucleotide synthesis.

A person of ordinary skill in the art would have been motivated at the time of the invention to use methylamino group modified polypropylene matrix to synthesize oligonucleotides, because solid state synthesis of oligonucleotides require modifying the solid support (matrix) to attach the synthesized oligonucleotides as taught by both Matson et al (who teach derivatizing the solid support for attaching polynucleotide in Column 5, lines 40+), and

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Meldal teaches using polypropylene polymer comprising methylamino group for attaching oligonucleotides thereon as discussed above.

A person of ordinary skill in the art would have been motivated at the time of the invention to use 3'-succinate derivative of protected nucleosides to synthesize oligonucleotides, because Kierzek et al teach a rapid method for synthesizing oligoribonucleotides on a solid-phase support by using succinate derivative of protected nucleosides (see pg 7840, left col., 1<sup>st</sup> para.), and Fernandez-Fornier et al teach a rapid and efficient preparation of oligonucleotides using p-nitrophenylethyl (such as NPEOC) type base protecting groups.

An ordinary skilled artisan would have reasonable expectation of success of achieving such modifications since Meldal has demonstrated the successful modification of polypropylene matrix with methylamino group and Kierzek et al and Fernandez-Fornier have demonstrated the successful utilization of 3'-succinate derivative of protected nucleosides for solid state synthesis of polynucleotides.

17. Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being obvious over Weiler et al (Nucleosides and Nucleotides. Vol. 14(3-5):917-920; 1995), Matson et al (US 5,429,807; 7/4/1995), and Meldal et al (US Patent 5,352,756; 10/4/1994).

**Weiler et al**, throughout the publication, teach an automated method for large scale synthesis of oligonucleotides applying the NPE/NPEOC-strategy, as discussed supra.

Weiler et al do not specifically teach the polymer matrix is polypropylene as recited in **clm 7**, and the matrix is modified with methylamino groups as recited in **clm 2**.

However, **Matson et al**, throughout the patent, teaches an automated method and apparatus for performing biopolymers (oligonucleotide) synthesis (see Abstract of the reference), which readson the automated synthesis of **clm 1**. The reference teaches that the solid support for attaching polynucleotides is polypropylene (see Claim 20 of the reference), which reads on the polypropylene polymer matrix of **clms 1, 5 and 7**. The reference also teaches parallel polynucleotide syntheses with a plurality of parallel channels (col. 3, lines 45+ and Claims 15 and 20 of the reference), which read on the multichannel synthesis chamber with fixed matrix, as recited in **clm 4**.

**Meldal**, throughout the patent, teaches polypropylene glycol-containing polymer designed for the application of a solid support for the oligonucleotide synthesis (see Abstract of the reference). The reference also teaches a spacer linked to the polymer comprises a methylamino group (see Figure 2 and Claim 4, formula II of the reference), which reads on the methylamino group modified matrix surface, as recited in **clm 2**.

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use polypropylene matrix derivatized with methylamino groups and 3'-succinate derivative of protected nucleosides for automated polynucleotide or oligonucleotide synthesis.

A person of ordinary skill in the art would have been motivated at the time of the invention to use polypropylene as matrix to support the solid phase synthesis of oligonucleotides, because Matson et al teaches that particular and suitable solid phase supports such as polypropylene are used for solid state oligonucleotide synthesis (col. 1, lines 15+ and col. 4, lines 60+). A person of ordinary skill in the art would have been motivated at the time of the

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invention to use DNA synthesizer with parallel multichannels to efficiently synthesize multiple oligonucleotides with different sequences as taught by Matson et al (col. 1, lines 55+).

A person of ordinary skill in the art would have been motivated at the time of the invention to use methylamino group modified polypropylene matrix to synthesize oligonucleotides, because solid state synthesis of oligonucleotides require modifying the solid support (matrix) to attach the synthesized oligonucleotides as taught by both Matson et al (who teach derivatizing the solid support for attaching polynucleotide in Column 5, lines 40+), and Meldal teaches using polypropylene polymer comprising methylamino group for attaching oligonucleotides thereon as discussed above.

An ordinary skilled artisan would have reasonable expectation of success of achieving such modifications since Meldal has demonstrated the successfully modification of polypropylene matrix with methylamino group and Matson et al have demonstrated the successful utilization poly propylene as solid state synthesis matrix in a multi-channel automated system for synthesis of polynucleotides.

18. Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being obvious over Weiler et al (Innovation Perspect. Solid Phase Synth. Collect. Pap., Int. Symp., 3rd (1994), Meeting Date 1993, pg 131-134. Editor(s): Epton, Roger. Mayflower Worldwide Ltd.: Birmingham, UK), and Matson et al (US 5,429,807; 7/4/1995).

**Weiler et al**, throughout the publication, teach an automated method for large scale synthesis of oligonucleotides applying the NPE/NPEOC-strategy, as discussed supra.



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Weiler et al do not specifically teach the polymer matrix is polypropylene as recited in **clm 7**.

However, **Matson et al**, throughout the patent, teaches an automated method and apparatus for performing biopolymers (oligonucleotide) synthesis (see Abstract of the reference), which readson the automated synthesis of **clm 1**. The reference teaches that the solid support for attaching polynucleotides is polypropylene (see Claim 20 of the reference), which reads on the polypropylene polymer matrix of **clms 1, 5 and 7**. The reference also teaches parallel polynucleotide syntheses with a plurality of parallel channels (col. 3, lines 45+ and Claims 15 and 20 of the reference), which read on the multichannel synthesis chamber with fixed matrix, as recited in **clm 4**.

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use polypropylene matrix derivatized with methylamino groups and 3'-succinate derivative of protected nucleosides for automated polynucleotide or oligonucleotide synthesis.

A person of ordinary skill in the art would have been motivated at the time of the invention to use polypropylene as matrix to support the solid phase synthesis of oligonucleotides, because Matson et al teaches that particular and suitable solid phase support such as polypropylene are used for solid state oligonucleotide synthesis (col. 1, lines 15+ and col. 4, lines 60+). A person of ordinary skill in the art would have been motivated at the time of the invention to use DNA synthesizer with parallel multichannels to efficiently synthesize multiple oligonucleotides with different sequences as taught by Matson et al (col. 1, lines 55+).

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An ordinary skilled artisan would have reasonable expectation of success of achieving such modifications because Matson et al have demonstrated the successful utilization of polypropylene as solid state synthesis matrix in a multi-channel automated system for synthesis of polynucleotides.


### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached at 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL  
Art Unit 1639  
7/21/2006

  
**MARK SHIBUYA, PH.D.**  
**PATENT EXAMINER**

|                         |                                    |                                      |  |
|-------------------------|------------------------------------|--------------------------------------|--|
| <b>Notice to Comply</b> | <b>Application No.</b><br>09202969 | <b>Applicant(s)</b><br>WEILER ET AL. |  |
|                         | <b>Examiner</b><br>Sue Liu         | <b>Art Unit</b><br>1639              |  |

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other:

**Applicant Must Provide:**

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application.**
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510

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